

"APPROVED FOR RELEASE: 09/19/2001

CIA-RDP86-00513R001343320012-2

1956 -

APPROVED FOR RELEASE: 09/19/2001

CIA-RDP86-00513R001343320012-2"

Michalav Prokopa

(Sulfonium salts of high spasmolytic activity. Michalav Prokopa and Jiri O. Jilek. Czech. 85,855, Aug. 15, 1958. Catalyzed reesterification of esters of substituted phenylacetic acid with 2-alkylmercaptoethanols followed by addn. of alkyl halides to the intermediary products gives compds. with high bioi. activity and avoids the troublesome operations described in Czech. 83,205 (C.A. 50, 7140h). Adding portionwise 0.0 g. Na to 22.0 g. 2-methylmercaptoethanol (I) with cooling and stirring, treating the soln. with 15.5 g. Et ester of phenylcyclohexylacetic acid, heating the mixt. slowly to 150-60° in an oil bath and maintaining this temp. for 30 hrs. with removal of EtOH, distg. excess I, shaking the residue with H₂O and extg. with Et₂O gives, on distn. in vacuo, 2-methylmercaptoethyl ester of phenylcyclohexylacetic acid, b.p. 150-70° which gives, when left with MeI in a sealed flask 48 hrs. in the dark, in quant. yield 2-(phenylcyclohexylacetoxymethyl)dimethylsulfonium iodide, m. 102° (EtOH). L. J. Urbánek

2

PROTIVA, 141105-17V

2
 Sulfonium salts of high spasmolytic activity. Miroslav
 Protiva and Edita Adlrová. Czech, 85,856, Aug. 15, 1956.
 Condensation of metal salts of substituted mandelic acids
 with 2-haloethylalkyl sulfides followed by addn. of alkyl
 halides to the intermediate sulfide ester products gives
 compds. with high biol. activity. The introduction of an
 OH group into the mol. raises the parasympatholytic and
 anticholinergic effect of these compds. and lowers their
 toxicity in comparison with compds. described in Czech.
 83,205. An improved soly. in H₂O suggests their use by
 injection. Dissolving 12 g. α-propylmandelic acid in a
 soln. of EtONa prepd. from 1.4 g. Na and 61 ml. abs.
 EtOH, adding 7.5 g. MeSCiH₇CH₂Cl (1), refluxing 4 hrs.,
 cooling, sepg. the pptd. salt, evapg. the filtrate *in*
vacuo, and distg. gives 11.6 g. 2-methylmercaptoethyl ester

Protiva, M.

CZECHOSLOVAKIA/Pharmacology and Toxicology - Muscle Relaxants

V

Abs Jour : Ref Zhur - Biol., No 2, 1959, 9140

Author : Borovicka, M., Cimler, L., Protiva, M.

Inst : -

Title : Two New Patterns of the Molecular Structure of d-Tubocurarine Chlorides.

Orig Pub : Chemotherapeutika. I. Farmac. sympos., Praha, 1956, 51-52.

Abstract : No abstract.

CZECHOSLOVAKIA/Chemical Technology. Chemical H
Products and Their Applications.
Medicinal Substances. Vitamins.
Antibiotics.

Abs Jour : Ref Zhur-Khimiya, No 6, 1959, 20548

Author : Protiva, Miroslav

Inst :

Title : Some Remarks on the Nomenclature of Organic
Medicinal Substances in the Czechoslovakian
Pharmacopoeia 2.

Orig Pub : Ceskosl. farmac., 1956, 6, No 9, 559-561

Abstract : No abstract.

Card : 1/1

PROTIVA, M., AND others.

PROTIVA, M. and others. Synthetic experiments in groups of estrogenic hormones. VIII. Chemistry of 2-methyl-4-carboxy-6-oxycyclohexanone derivatives. In German. p. 159. Vol. 21, No. 1, Feb. 1966. Sborník československých chemických zpráv. COLLECTION OF CZECHOSLOVAK CHEMICAL COMMUNICATIONS. Praha, CZECHOSLOVAKIA.

SOURCE: EAST EUROPEAN ACCESSIONS LIST (EPAL VOL 6, NO 4, APRIL 1967)

PASTHA MIROSLAV

Chem ✓ Syntheses in the estrogenic hormone group. X. Some derivatives of 6-methoxy-2-acetonaphthone and 8-(6-methoxy-2-naphthoyl)propionic acid. Ludvík Novák and Miroslav Protička (Pharm. and Biochem. Research Inst., Prague). *Chem. Zvesti* 30, 1010-10 (1958); cf. C.A. 51, 2837g. — A series of compds. serving as intermediary products in the synthesis of bisdehydrodissynolic acids was prepd. [In this abstr. R = 6-methoxy-2-naphthyl throughout.] Contrary to Robinson (C.A. 34, 770^g), the prepn. of RAc (I) from 384 g. nerolin yielded in addn. to 63 g. I, 8 g. crystals, m. 189°, apparently of MeCH₂CH:CHCOR. Attempts to introduce a carboxyl function into the α-position of I by treating 40 g. I at 60° with 88 g. (CO₂Et)₂ and dry MeONa (4.6 g. Na) in 160 ml. dry C₆H₆, heating 8 hrs. on a water bath, and decompg. with dil. H₂SO₄, failed because the RCOCH₂COCO₂Et (49.3 g.), m. 125°, obtained could not be decarboxylated till at 210-30°, at which temp. the resulting RCOCH₂CO₂Et (II) was not stable. II was obtained in 51-g. yield by dropping with stirring 40 g. I in 150 g. CO(OEt)₂ into a boiling mixt. of 4.6 g. Na in 100 g. CO(OEt)₂, distg. off the EtOH split off, pouring the mixt. into dil. AcOH, and extg. the II with Et₂O. Crude oily II, characterized as the 1,4-dinitrophenylhydrazone, m. 207° (from pyridine-ligroine), could not be further purified since it decompd. on distn. to give a yellow compd., m. 248° (from xylene), apparently 3-(6-methoxy-2-naphthoyl)-6-(6-methoxy-2-naphthyl)pyrone. Alkylation of 13.6 g. crude II by refluxing 5 hrs. with 1.1 g. powd. Na in 100 ml. C₆H₆, and then 4 hrs. with 8.3 g. BrCH₂CO₂Et gave 7.1 g. oil, b.p. 220-30°, which, without characterization, refluxed 3 hrs. with 0.5 g. Na in

2

1/2

Novák, Ludvík; Penta, Hroslav

60 ml. abs. MeOH and 5.0 g. MeI yielded 4.6 g. RCO_2Me , m. 123°. $RCOCH_2Br$ (III), obtained in 27-g. yield from 20 g. I in 100 ml. dry Et_2O with 16 g. Br in the presence of $AlCl_3$, m. 123° (from AcOEt); 1.4 g. III ground with 2.2 g. CuCN, heated 4 hrs. to 180°, and the product extd. with 100 ml. boiling C_6H_6 and treated with 100 ml. 12% aq. NH_4OH yielded, on recrystn., 0.8 g. $RCOCH_2CN$, m. 190° (from AcOEt). A mixt. of 2.5 g. $RCOCH_2CH_2CO_2H$ (IV) and 30 ml. Ac_2O refluxed 1 hr. and poured into water gave 1.8 g. γ -(6-methoxy-2-naphthyl)- Δ^2 - γ -butenolide, m. 181-2°. IV Me ester (13.5 g.) condensed with 11.8 g. $(CO_2Me)_2$ in the presence of dry MeONa gave, instead of the expected substituted pyruvate, 6.2 g. RCO_2Me , m. 126° (from MeOH). Bromination of 5.4 g. IV Me ester with 1.1 ml. Br in Et_2O and CCl_4 gave 5.1 g. $RCOCHBrCH_2CO_2Me$, m. 179° (from C_6H_6).

L. J. Urbánek 2/2.

Mykalszyn, V., Jilek, J.O., Protiw, M.

phenyl ketone (picrate, m. 180°) as by-products. V was dehydrated by boiling 2 hrs. with 1:1 H₂SO₄ to 1-dimethyl-amino-3-benzhydrylidencyclohexane, insol. in Et₂O and C₆H₆, picrate, m. 186° (from EtOH); HCl salt, m. 227° (from EtOH-Et₂O). IV and V had very low anticholinergic and antihistaminic activity and LD₅₀ = 82 mg./kg. and 91 mg./kg., resp.

L. J. Urbánek

3/2

PROTIVA, MIROSLAV

7
1
Synthetic analogs of the curare alkaloids. VII. Two new tubocurarine models and two bisquaternary simonolium salts. Miroslav Protiva, Milos Horvick, Lasa Cimlik, and Zdenek Sedivy (Pharm. Biochem. Research Inst., Prague). *Chem. Listy* 50, 1959-64 (1956); cf. C.A. 51, 2622d. — 1,10-Diaminocyclooctadecane (I), obtained in 3.1-g. yield by adding 6.6 g. Na to 3.7 g. cyclooctadecane-1,10-dione dioxime in 60 ml. boiling abs. EtOH, evap. the EtOH and extg. with Et₂O, was distd., b.p. 180-5°; dipicrate m. 238-40° (from dild. Me₂CO). I (2.0 g.), 25 ml. MeOH, 1.72 g. KOH, and 12 g. MeI was left overnight and refluxed 7 hrs. with gradual addn. of further 6 g. MeI; evapd. to dryness, extd. with hot Me₂CO, and crystd. from iso-PrOH to give 1.7 g. colorless platelets of the dimethiodide of 1,10-bis(dimethylamino)cyclooctadecane (II) which did not melt below 300°. Cyclooctadecane-1,10-diol, obtained in 7.2-g. yield by reducing 9.0 g. cyclooctadecane-1,10-dione with 1.8 g. LiAlH₄ in Et₂O-C₆H₆, was recrystd. from Me₂CO, m. 120-30°, and refluxed 3 hrs. with Ac₂O to give 83% cyclooctadecane-1,10-diol diacetate m. 72-3° (from aq. EtOH). *p*-Me₂N(CH₂)₂OC₆H₄CH₂CN (III) obtained in 15.8-g. yield by dropping in EtOH soln. of 40 g. *p*-HOC₆H₄CH₂CN (IV) into EtONa prepd. from 7.0 g. Na and 100 ml. abs. EtOH and refluxing the resulting IV Na salt with 40 g. Me₂N(CH₂)₂Cl 5 hrs., was extd. with CHCl₃ and distd., b.p. 135-7°; picrate, m. 102-2.5° (from H₂O); HCl salt, m. 156-7° (from EtOH-Et₂O). III (15.8 g.) in 100 ml. MeOH was satd. at 6° with NH₃ and hydrogenated

Protiva, M., Boravicko, M., Cisker, L., ...

by shaking with 3 g. Raney Ni 5 hrs. in an autoclave at 90-100° and 100 atm. to 11.1 g. oily $Me_2N(CH_2)_2OC_6H_4(CH_2)_2NH_2$ (V), b_p 120°; dipicrate, m. 109-70°; 1-Az deriv., b_p 175-7°, m. 20-2° (from ligroine). V (3.0 g.) with 12.2 g. MeI in MeOH-NaOH gave 7.9 g. $[Me_2N^+(CH_2)_2OC_6H_4(CH_2)_2N^+Me_2]2I^-$ (VI), m. 206-2° (decompn.) (from aq. EtOH). 1-Phenyl-2-(4-cyanomethylphenoxy)propan-1-one (VII), obtained in 14-g. yield by refluxing the Na salt of 13.3 g. IV with 21.3 g. BzCHMeBr (VIII) 7 hrs. in EtOH, was extr. with Et₂O and fractionated by distn., b_{0.5} 203-12°, m. 70-30.5° (from iso-PrOH). VII could not be converted to a diamine. An analogous condensation of 13.3 g. IV with 21.3 g. VIII gave as sole product Bz(CH₂)₂OEt. II revealed a high curare activity which was qualitatively near to the effect of d-tubocurarine chloride; VI was considerably less potent. 1,4-Bis(dimethylamino)-2-(2,5-dimethoxyphenyl)butane-2MeI, m. 233-40°, obtained in 3.5-g. yield by refluxing 8 hrs. 2.8 g. 1,4-diamino-2-(2,5-dimethoxyphenyl)butane with 21.3 g. MeI in MeOH, and 1,5-dipiperidinopentane-2MeBr, m. 258-9° (decompn.), prepd. in 160-g. yield by refluxing 7 hrs. 212 g. N-methylpiperidine, 228 g. Br(CH₂)₃Br, and 400 ml. iso-PrOH, were synthesized as compds. with possible ganglioplegic activity.

L. J. Ustunel

PROTIVA, MIROSLAV

G-2

: CZECHOSLOVAKIA/Organic Chemistry - Synthetic Organic Chemistry.

Abs Jour: Referat Zhur-Khimiya, No 5, 1958, 14426

Author : Jilek Jiri O., Protiva Miroslav

Inst :

Title : Synthetic Spasmolytic Agents. XV. New Methods for the Preparation of Hexadiphenylsulfonium Iodide.

Orig Pub: Ceskosl. farmac., 1957, 6, No 2, 113-119.

Abstract: $RSCH_3$ (I), wherein $R = C_6H_5CH(C_6H_{11})COOCH_2CH_2$ throughout, necessary for the preparation of active spasmolytic RS^+ $(CH_3)_2I^-$ (II), was obtained by three methods: by ester interchange of $C_6H_5CH(C_6H_{11})CO-OC_2H_5$ (III, acid IIIa) with $CH_3SCH_2CH_2OH$ (IV) (with a poor yield); by condensation of IIIa with $CH_3SCH_2CH_2Cl$ (V); by condensation of the 2-brom-ethyl ester of IIIa (VI) with CH_3SNa . VI was prepared by condensation of IIIa with $C_2H_4Br_2$ (VII) in acetone; analogously from IIIa and VII in alcohol is obtained the 2-hydro-

Card : 1/3

CZECHOSLOVAKIA/Organic Chemistry - Synthetic Organic Chemistry.

G-2

Abs Jour: Referat Zhur-Khimiya, No 5, 1958, 14426.

xyethyl ester of IIIa (VIII). Also prepared were $\text{RSC(=NH)NH}_2 \cdot \text{HBr}$ (IX) and $\text{HOCH}_2\text{CH}_2\text{S}^+(\text{CH}_3)_2\text{I}^-$ (X). In the synthesis of phenyl-cyclohexyl-acetonitrile (XI) (see Biel J. H. et al., J. Amer. Chem. Soc., 1952, 74, 1485) there was obtained, as a byproduct, phenyl-dicyclohexyl-acetonitrile, MP 134° (from alcohol; all melting points are corrected). By heating (110-120 $^\circ$, 3 hours) 21.8 g III [IIIa] with 46 g alcohol and 10 g 100% H_2SO_4 , III was obtained with a 55% yield, BP $130^\circ/1.6$ mm. On boiling for 8 hours 15 g XI with 15 ml alcohol, 9 ml H_2SO_4 and 6 ml water, and diluting with water, there are obtained 12.5 g phenyl-cyclohexyl-acetamide, MP $165-167^\circ$. Mixture of 105 g IIIa, $\text{C}_2\text{H}_5\text{ONa}$ (from 10.85 g Na and 480 ml absolute alcohol) and 60.2 g V is kept for 10 hours at 0° , and boiled for 10 hours, to get 82.5% I, BP $165-166^\circ/1.3$ mm, MP $29-30^\circ$. From 19 g I and 5 ml CH_3I were obtained 22.2 g II, MP $101-102^\circ$.

Card : 2/3

CZECHOSLOVAKIA/Organic Chemistry - Synthetic Organic Chemistry.

G-2

Abs Jour: Referat Zhur-Khimiya, No 5, 1958, 14426.

From 25 g VI and 5.4 g CH_3SNa in 30 ml acetone (boiled 2.5 hours) I was obtained with a yield of 70%. Mixture of 39 g IIIa, 36 g K_2CO_3 , 200 ml acetone and 90 g VII, boiled 15 hours to get 70% VI, BP 155-159/0.5 mm, and 4.5 g $\text{C}_6\text{H}_5\text{CH}(\text{C}_6\text{H}_{11})\text{COOR}$, MP 78° (from alcohol). 5.2 g VIII (MP 73-74° (from acetone)) are obtained by boiling for 24 hours a mixture of 21.8 g IIIa, 8.05 g $\text{HOCH}_2\text{CH}_2\text{Cl}$, 10.5 g KHCO_3 and 100 ml acetone. From 3.5 g VI, 3 ml alcohol and 0.8 g thiourea (6 hours, 120°) are obtained 4.1 g IX, MP 155° (from 70% CH_3OH). X is obtained with a good yield on allowing a mixture of 1 ml IV and 2 ml CH_3I to stand for 12 hours, MP 55° (from alcohol-acetone). Communication XIV, see RZhKhim, 1957, 47916.

Card : 3/3

CZECHOSLOVAKIA / Organic Chemistry. Synthetic Organic G-2
Chemistry.

Abs Jour: Ref Zhur-Khimiya, 1958, No 17, 57441.

Author : Borovicka M., Protiva M.

Inst : Not given.

Title : Synthetic Antispasmodic Remedies. XVI. Derivatives
of 3-Phenylindanone and 1-Amine-3-Phenylindan.

Orig Pub: Ceskosl. farmac., 1957, 6, No 3, 129-132.

Abstract: For the purpose of investigating pharmacological
properties, various substances were synthesized
using 3-phenylindanone (I) as a starting material.
These compounds comprised materials of the general
formula (II) and methyl ether of the 3-phenylinda-

Card 1/5

CZECHOSLOVAKIA / Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khimiya, 1958, No 17, 57441.

Abstract: non-1-glyoxinic-2 acid (III). The iodo-substitutes of II, ie IIb, IIc, and IIg exhibited weak antihistamine and antispasmodic activities. A solution containing 10.5gr IIa (derived from I and LiAlH_4 with 75% yield, boiling point of 135-136°/0.35mm and melting point of 79-80°) in C_6H_6 is boiled for 1 hour with 4gr NaNH_2 , after adding 8.1gr of $\text{ClCH}_2\text{CH}_2\text{N}(\text{CH}_3)_2$, is boiled for 5 additional hours. The obtained IIb yield is 71%, 165-167°/1.4 mm boiling point; iodomethylate has melting point of 185-186°. 18.5gr of II oxime (141-142° melting point) is hydrated in CH_3OH over Ni at 80-90°, and 100atm. pressure for 8 hours. The yield of IIC is 67%, 154°/4mm and 135-140°/0.4mm boiling point.

Card 2/5

CZECHOSLOVAKIA / Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khimiya, 1958, No 17, 57441.

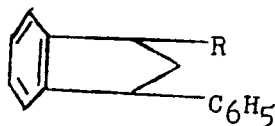
Abstract: Its chlorhydrate and picrate have melting points of 224-225° and 218-220° respectively. Solution containing 1.gr NaOH, 3gr IIc, and 15gr CH₃I in 45cc CH₃OH is boiled, followed by the addition of 6.4gr of CH₃I, by evaporation (8 hours), and by precipitation in acetone 18gr of II d of 197-198.5° melting point are formed. From 2.09gr of the obtained II c and 1.06gr of C₆H₅CHO (boiling in alcohol for 4 hours), 69% yield of II e (of 100-101° melting point) is obtained. Upon hydrogenation over Ni, 85% yield of IIh (of 80-81° melting point) is obtained. Its chlorhydrate and picrate have

Card 3/5

CZECHOSLOVAKIA / Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khimiya, 1958, No 17, 57441.

Abstract: melting points of $216-218^{\circ}$ and $197-198^{\circ}$ respectively. II g is produced analogically, from II h using C_2H_5OH . Yield is 71% and melting point is $185-186^{\circ}$. Dry CH_3ONa (obtained from 0.92gr of Na) is boiled for 30 minutes with 4.72gr $CH_3OCOCOONa$ in C_6H_6 , to which 4.19gr of I is then added followed by boiling for 1 hour, by the decomposition with water and by the separation of III with 2% NaOH. The obtained yield of III is 55% of $214-216^{\circ}$ melting point. General key of structure of the compounds involved is shown as follows:



Card 4/5

CZECHOSLOVAKIA / Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khimiya, 1958, No 17, 57441.

Abstract: a: $R = OH$; b: $R = OCH_2CH_2N(CH_3)_2$; c: $R = NH_2$;
d: $R = N(CH_3)_2I$; e: $R = C_6H_5CH N$; h: $R = C_6H_5CH_2NH$;
g: $R = C_6H_5CH_2N(CH_3)_2I$.
For Part XV refer to Ref Zhur-Khimiya, 1958, 14426.

Card 5/5

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khim., No 13, 1958, 43414.

Author : Novak Ludvik, Srnkova Jirina, Votava Zdenek,
Protiva Miroslav.

Inst :

Title : Antihistaminic Agents. XXXIX. Synthesis and Pharmacological Properties of the Hydrochloride of N-(1-Methyl-3-Piperidyl-methyl)-Phenothiazine.

Orig Pub: Ceskosl. farmac., 1957, 6, No 7, 365-369.

Abstract: The hydrochloride of N-(1-methyl-3-piperidylmethyl)-phenothiazine (I) has been synthesized, which is identical with the German antihistaminic preparation Pakatal' [transliterated], and its pharmacological properties have been tested in comparison with chlorpromazine. I possesses effective local

Card : 1/4

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khim., No 13, 1958, 43414.

anesthetic action in surface analgesia, counteracts toxic effect of pentasol (in mice), does not enhance thiopental narcosis (mice-rabbits), on peroral administration the toxicity of I is lower than that of chlorpromazine, body temperature (mouse) is lowered less by the action of I than by that of chloro-promazine, I does not enhance the anticonvulsant action of Mesantoin. 135.9 g ethyl ester of nicotinic acid are hydrogenated in CH_3COOH at 20° and 120 atmospheres with 2.25 g Pt (from PtO_2), the product thus obtained is hydrogenated further, without being isolated, with 100 g 30 % formalin and 10 g 10% Pd/C at 110 atmospheres. Fractionation yields 72 g ethyl ester of N-methylpiperidine carboxylic acid-3 (II), BP 90-91/10 mm; hydrochloride,

Card : 2/4

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khim., No 13, 1958, 43414.

MP 136°. 39 g II are reduced with 21.4 g Na in 34 g n-butanol and 200 ml toluene, to get 1-methyl-3-piperidylcarbinol (III), yield 68%, BP 105/10 mm. By treatment of 10.2 g III-hydrochloride with 38 g SOCl_2 was prepared the hydrochloride of 1-methyl-3-chloromethyl-piperidine (IV), yield 70%, MP 163°. To freshly prepared NaNH_2 (5.7 g Na, 500 ml liquid NH_3) are added dropwise 350 ml xylene and then 21.7 g phenothiazine, NH_3 is evaporated, residue boiled 1 hour, 21 g IV added, boiled for 20 hours, fractional distillation permits isolation of N-(1-methyl-3-piperidylmethyl)-phenothiazine, yield 82%, BP 190/0.8 mm; HCl-salt of monohydrate of I, MP 172-

Card : 3/4

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khim., No 13, 1958, 43414.

174⁰; oxalate, MP 222-223⁰. Communication XXXVIII
see RZhKhim, 1955, 31657.

Card : 4/4

PROTIVA, M.

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64383.

Author : Protiva, Mychajlyszynv, Novakl, Borovickam,
Adlerovae, Hachv.

Inst :

Title : Synthetic Spasmolytic Agents. XVII. Certain New
Esters and Amides Containing a Sulfonium Group.

Orig Pub: Ceskosl. farmac., 1957, 6, No 8, 425-431.

Abstract: To test for spasmolytic activity, sulfonium salts
were extracted from the sulfides $\text{CH}_3\text{SCH}_2\text{COR}$ (I),
 $\text{CH}_3\text{SCH}_2\text{CH}_2\text{COR}$ (II), $\text{CH}_3\text{CH}(\text{SCH}_3)\text{COR}$ (III), where
(a) R is OC_2H_5 , (b) OH, (c) Cl, (d) $\text{OCH}(\text{C}_6\text{H}_5)$.
During in vivo tests, the iodo-methylates of (IIId),
(II) R = $(\text{C}_6\text{H}_5)_2\text{N}$, (IIe), (II), R = $\text{C}_6\text{H}_5\text{CH}_2\text{NC}_2\text{H}_5$, (IIIf),

Card : 1/6

17

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64383.

as well as the iodide $\text{[C}_6\text{H}_5\text{CH}_2\text{COOCH}_2\text{CH}_2\text{S(CH}_3\text{)}_2\text{]I}$ (IV) proved effective.

(Ia), (IIIa), (Id) and (IIId) decompose under the action of CH_3I , and do not form iodo-methylates.

To a boiling solution of CH_3SNa (V) (made from 175 g. of the sulfate $\text{H}_2\text{NC(=NH)SNa}$), in .5 liters of ethanol, are added 122 g. of $\text{ClCH}_2\text{COOC}_6\text{H}_5$). Boil 2 hours, concentrate in a vacuum, add water, and recover (Ia) in ether, yield 65%, b.p. 57-62°/10 mm. In the same way there can be produced (IIIa), yielding 56% and (IIa), yielding 70%, iodo-methylate, m.p. 123°. 86 g Ia and 200 ml of 20% NaOH are boiled one hour, 120 ml of concentrated HCl are added and ex-

Card : 2/6

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64383.

tracted with ether 72% Ib, boiling point 108-112°/8mm. Obtained in the same way are 80% IIb, boiling point 105-108°/8 mm, 70% IIB, boiling point 120-124/8mm. To 10.6 g of Ib 20 ml of SOCl₂ is added, boiled one hour, Iv is distilled, 80%, boiling point 57-60°/15 mm. Obtained analogously are 65% III, boiling point 95-100°/100 mm, 58% IIv, boiling point 77-82°/8 mm. To 8 g (C₆H₅)₂CHOH in 35 ml of C₆H₆ and 30 ml of pyridine, 7 g Ic in 35 ml of C₆H₆ is added at 0° for 15 minutes, from the solution are yielded 7 g Id, boiling point 153-155°/0.4 mm. IIId, boiling point 147-149°/0.2 mm; IIId, boiling point 169-172°/0.7 mm, melting point 38°, iodo-methylate, melting point 107°. From 27.2 g C₆H₅CH₂COOH and iso-C₃H₇MgCl by a well-known method (RZhKhim, 1957 26740) is obtained 19 g of 1-oxicyclohexylphenylacetic acid

Card : 3/6

7

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry, G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64383.

(VI), melting point 132-133°, and 2.5 g of meso- α, β -diphenylsuccinic acid, melting point 224-225°. During the attempt to condense Na-salt VI with $\text{ClCH}_2\text{CH}_2\text{SCH}_3$ (VII) and the processing of the mixture CH_3I , only IV is yielded. $\text{C}_6\text{H}_5\text{CH}_2\text{COONa}$ (from 6.8 g of acid) and 6 g of VII are boiled 4 hours in 60 ml of absolute, the filtrate is distilled, of the processed fraction 150-152°/15 mm (4g) CH_3I , IV is obtained melting point 98.5-99.5. 3.25 g (cyclo- C_6H_{11}) $\text{CH}(\text{C}_6\text{H}_5)\text{COOCH}_2\text{CH}_2\text{Br}$ and 1.05 g of absolute pyridine is heated 3 hours at 100-120°, the $\text{CH}(\text{C}_6\text{H}_5)\text{COOCH}_2\text{CH}_2\text{NC}_5\text{H}_5/\text{Br}$ obtained is triturated with ether, melting point 103-105°, is very absorbent, in a water solution yields with $\text{NaClO}_4/\text{CH}(\text{C}_6\text{H}_5)\text{COOCH}_2\text{CH}_2\text{NC}_5\text{H}_5/\text{ClO}_4$, melting point 122-123°. 16.9 g $\text{C}_6\text{H}_5\text{NHCOCH}_2\text{Cl}$ is boiled with 11g of V in 100 ml of acetone

Card : 4/6

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64383.

15 hours, concentrated in a vacuum, water is added and C_6H_5 extracted. 52% I, $R = C_6H_5NH$, melting point 79° , during processing of CH_3I yields an adduct of iodo-methylate I, $R = C_6H_5NH$ and $(CH_3)_3SI$, melting point $130-131^\circ$. 4 g of 3-chlorophenothiazine is boiled with 3.1 g of $ClCH_2CH_2COCl$ in 50 ml of C_6H_6 , 4 hours, concentrated in a vacuum, 5.5 g of N-(β -chloropropionyl)-3-chlorophenothiazine is obtained, melting point $112-113^\circ$. The mixture 3.15 g of $C_6H_5N(C_2H_5)COCH_2CH_2Cl$, 1.5 g of V and 50 ml of acetone is boiled 10 hours, diluted with water and extracted with ether of II, $R = C_6H_5NC_2H_5$ (IIh). From unrefined IIh and CH_3I in acetone iodo-methylate of IIh is obtained, melting point 98° . From 13 g $(C_6H_5)_2NCOCH_2CH_2Cl$ and 4.2

Card : 5/6

9

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64383.

g of V in acetone (boiling 10 hours) 78% of IIId is obtained, boiling point 168-175°/0.6 mm, melting point 63-64°, iodo-methylate, melting point 111-112.5°. Analogously from $C_6H_5CH_2N(C_6H_5)COCH_2CH_2Cl$ is obtained IIIf, boiling point 190°/1.6 mm, melting point 59-60°, iodo-methylate, melting point 107-108°. In the same way from N-(β -chloropropionyl)-phenothiazine is obtained II, R = N-phenothiazine, yield 61%, boiling point 230-235°/1 mm, melting point 78°, iodo-methylate, melting point 131-132°. Report XVI, see RZhKhim, 1958, 57441.

Card : 6/6

PROTIVA, M.

Pharmaceutical symposium in Prague.

P. 141 (Chemie, Vol 9, no. 1, Apr. 1957, Praha, Czechoslovakia)

Monthly Index of East European Accessions (EFAI) LC. Vol. 7, no.2, February 1958

✓ A new total synthesis of a racemic polystyrollic acid M. Mayak P.S.

The methyl- β -lactone-3-carboxylic acid (I) was obtained by treatment of II with CH_3N . The lactone gave the corresponding ester (III); semicarbazide of III, diethylphenylhydrazine, m. 138°. It was treated with N-methyl-pyrrolidylacetamide in *tert*-BuOH giving a good yield of the acetylene deriv., $\text{C}_{10}\text{H}_{16}\text{O}$, which, in the presence of Pd was hydrogenated quantitatively with 2 moles H to give 10% compd. (III), $\text{C}_{10}\text{H}_{20}\text{O}$, m. 79°. III was identified as the lactone of 1-(m-methoxyphenylethyl)-2-ethyl-3-methylcyclohexanecarboxylic acid. III was cyclized in boiling benzene with HCl and NH_4Cl giving a good yield of an amorphous partially demethylated carboxylic acid (IV). IV was methylated in alk. soln. with Me_2SO and then esterified with CH_3N ; presumably to Me 1-ethyl-2-methyl-7-methoxy-1,2,3,4,9,10,11,12-octahydro-

Km na

Protyva, M.

Distys 103d

10

Pharmacodynamically interesting aminoalkyl derivatives of acridan and phenothiazine homologs. M. Protyva, M. Borovička, V. Hach, Z. Volava, J. Šimková, and Z. Hornáková (Výzkumný ústav farm. a biotech., Prague). *Experientia* 13, 201-2 (1967) (in German).--Homoaacridan (I) (hydrochloride, m. 188-90°) was obtained by the reduction and simultaneous hydrogenolysis of 2'-amino-6-phenyl-2-carboxylic acillactam with LiAlH_4 . Homophenothiazine (II) (m. 115°; hydrochloride, m. 173°) was obtained by cyclizing 3'-amino-2-methoxycarbonyldiphenylsulfide (m. 95-6°; picrate, m. 167°), obtained from the corresponding nitro ester, and reducing the resulting lactam (m. 230-42°) with LiAlH_4 . I and II were made to react with substituted aminoalkyl chlorides in the presence of NaNH in toluene or xylene to give the following: *N*-(dimethylaminoethyl)-1-aza-2,3,5,6-dibenzocycloheptadiene (III), hydrochloride, m. 200°; *N*-(diethylaminoethyl)-1-aza-2,3,5,6-dibenzocycloheptadiene (IV), dihydrochloride, m. 164°; *N*-(piperidinoaminoethyl)-1-aza-2,3,5,6-dibenzocycloheptadiene (V), dihydrochloride, m. 209°; *N*-(dimethylaminopropyl)-1-aza-2,3,5,6-dibenzocycloheptadiene (VI), hydrochloride, m. 183°; *N*-(dimethylaminoethyl)-1-aza-4-thia-2,3,5,6-dibenzocycloheptadiene (VII), hydrochloride, m. 206°; *N*-(piperidinoaminoethyl)-1-aza-4-thia-2,3,5,6-dibenzocycloheptadiene (VIII), succinate, m. 151°; *N*-(dimethylaminopropyl)-1-aza-4-thia-2,3,5,6-dibenzocycloheptadiene (IX), hydrochloride, m. 167°. VI has antihistaminic activity 800 times as great as that of 2-(diphenylmethoxy)-*N,N*-dimethylethylamine-HCl (X). The antihistaminic activities of III and VII are 10 times that of X. The local anesthetic effects (infiltration) of III-IX all exceed that of procaine; V and VII being the most effective. The local anesthetic effects (surface) of III-VII all exceed that of cocaine; VIII and IV being the most effective.

H. J. ... J. O. ...

... They were found to be highly active, as often as they

10
4E3d
4E4d

PROTIVA, M.; ADLEROVA, E.

"Synthetic antispasmodics. XIV. Two new parasympatholytically and spasmolytically highly active sulfonium salts. In German."

p. 1066 (Collection of Czechoslovak Chemical Communications. Sbornik Chekhoslovatskikh Khimicheskikh Rabot.) Vol. 22, no. 3, June 1957.
Prague, Czechoslovakia

SO: Monthly Index of East European Accessions (EEAI) LC. Vol. 7, no. 4,
April 1958

Protiva, M.

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry.

G-2

Abs Jour: Referat Zhur-Khimiya, No 4, 1958, 11219.

Author : Adlerova, E., Novak, L., and Protiva, M.

Inst :

Title : Syntheses of Members of the Estrogen Group. XIV. 2-Substituted Derivatives of 3-Methylcyclohexanone-3-Carboxylic Acid.

Orig Pub: Chem Listy, 51, No 3, 553-563 (1957) (in Czech)

Abstract: The action of 4-carbethoxy-3-methyl-2-cyclohexen-1-one (I) with C_2H_5Br and C_2H_5ONa (refluxing for 4 hrs in alcohol) yields 2-ethyl-3-methyl-4-carbethoxy-2-cyclohexene-1-one (II), yield 75% (when $NaNH_2$ is used, the yield of II is 42%), bp $139-143^\circ/10$ mm, which on alkaline hydrolysis gives 2-ethyl-3-methyl-2-cyclohexene-1-one (III), yield 55%, bp $89-95^\circ/12$ mm; semicarbazone (SC), mp $186-189^\circ$

Card : 1/6

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry.

G-2

Abs Jour: Referat Zhur-Khimiya, No 4, 1958, 11219.

(from aqueous alcohol); 2,4-dinitrophenylhydrazone (DNFH) mp 226-227° (from C₆H₅N). III is also formed in 70% yield by refluxing II with CH₃COOH and H₂SO₄. I and ClCH₂COOCH₃ in C₆H₆ (16 hrs reflux) in the presence of NaNH₂ gives 2-carboxymethyl-3-methyl-2-cyclohexene-1-one (IV), yield 35%, bp 171-176°/3 mm. Liquid IV is isolated in yields of 6.5% from crystalline IV, mp 109-110° (from petroleum ether). In a similar way I and Cl(CH₂)₂COCC₂H₅ give 2-(β-carboxyethyl)-3-methyl-2-cyclohexene-one (V), yield 42%, bp 171-176°/3 mm; the yield of crystalline V is 7.2%, mp 78.79° (from petroleum ether). Dihydroresorcinol (VI) and iso-C₄H₉OH in C₆H₆ in the presence of p-CH₃C₆H₄SO₃H gives 3-isobutoxy-2-cyclohexene-1-one (yield 53%, bp 110-120°/0.6 mm) which on reaction with CH₃MgI gives 3-methyl-2-cyclohexene-1-one, yield 22%, bp 80°/10 mm,

Card : 26

2

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Referat Zhur-Khimiya, No 4, 1958, 11219.

DNFH, mp 176-177° (from alcohol. The methylation of VI by a previously described method (H. Stetter and W. Dietrichs, Chem Ber, 85, 61 (1952)) yields 2-methyl-cyclohexane-1,3-dione (VII), mp 205-206° (from aqueous alcohol), which is converted to 2-methyl-3-isobutyloxy-2-cyclohexene-1-one (yield 78%, bp 98/0.2 mm); the latter on reaction with CH_3MgI gives 2,3-dimethyl-2-cyclohexene-1-one (VIII), yield 55%, mp 80-84°/10 mm; DNFH, mp 198-199° (from ethyl acetate). VII and ethylene glucol give 1,3-bis-ethylene ketal of VII, yield 39%, bp 137°/10 mm, which on reaction with 2,4-dinitrophenylhydrazine in alcohol in the presence of HCl (acid) is converted to the DNFH of the 1-ethylene ketal of VII, mp 163-164° (from alcohol). When a solution of 2.7 gms VIII in 25 ml CH_3OH is refluxed 3 hrs with a solution of 3.5 gms KCN in 20 ml

Card : 3/6

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Referat Zhur-Khimiya, No 4, 1958, 11219.

water, followed by the addition of a solution of 2.8 gms KOH in 50 ml water, heating for 30 hrs at 100°, and acidification, 3.7 gms of crude 3,2-dimethylcyclohexanone-3-carboxylic acid (IX) are obtained; DNPH, mp 222° (from CH₃OH-ethyl acetate). Reaction of IX with CH₂N₂ gives the methyl ester, yield 72%, bp 120°/10 mm; DNPH, mp 169° (from CH₃OH-ethyl acetate). The following compounds have been prepared by a similar procedure: 3-methyl-2-ethylcyclohexanone-3-carboxylic acid (X) (from III and KCN), yield 65%, mp 137-138° (from ether-CH₃OH); the methyl ester of X (XI) is obtained in yields of 79-92.5%, bp 142-143°/25 mm, 124-125°/20 mm, 92-93°/1 mm; SC of XI, mp 210-212° (from alcohol); DNPH of XI, mp 141° (from alcohol); 3-methyl-2-carboxymethylcyclohexanone-3-carboxylic acid (XII) (from IV and KCN), yield 65%, mp 160-163° (from

Card : 4/6

3

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Referat Zhur-Khimiya, No 4, 1958, 11219.

ethyl acetate-CH₃OH); the methyl ester of XII (XIII) is obtained in yields of 82%, bp 130-132°/1.8 mm; DNPH of XIII, mp 184-185° (from C₆H₆); 3-methyl-2-(β -carboxy-ethyl)-cyclohexanone-3-carboxylic acid (XIV) (from V and KCN), yield 80%, mp 119-123°; the methyl ester of XIV (XV) is obtained in yields of 67%, bp 135-142°/1 mm; DNPH of XV, mp 150.5-151.5° (from C₆H₆). XII and HS(CH₂)₂SH under the action of dry HCl and MgSO₄ in dioxane at 0° give the thioketal of XII, mp 210-211° (from CH₃OH) which on removal of the sulfur over Raney Ni gives an oily substance the structure of which has not been established. The Khuan-Minlon /TN: spelling uncertain/ reduction of XIII yields trans-2-methyl-2-carboxycyclohexylacetic acid, mp 171-173° (from petroleum etheracetone and aqueous CH₃

Card : 5/6

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Referat Zhur-Khimiya, No 4, 1958, 11219.

COOH). However, in view of the possibility of tautomerism during the Klemm-Minlon reduction, the trans-configuration of X-XV cannot be considered as definitely established. For Communication XIII see RZhKhim, 1957, 63629.

Card : 6/6

4

CZECHOSLOVAKIA/Organic Chemistry - Natural Compound and Their
Synthetic Analogs:

G.

Abs Jour : Ref Zhur - Khimiya, No 16, 1958, 54013

Author : Yilek, Protiva

Inst : -

Title : A Study of the Synthesis of Estrogenic Hormones. XV.
Reaction of Phenylacetylenes with Substituted Cyclo-
hexanones. A New Total Synthesis of Certain Racemic
Doisynolic Acids.

Orig Pub : Chem. listy, 1957, 51, No 4, 643-653

Abstract : 1-ethyl-2-methyl-7-hydroxy-1,2,3,4,9,10,11, 12-octahy-
drophenanthrenecarboxylic-2-acid (I) (from racemic
doisynolic acids) was synthesized in the following
manner:
The reaction of $m\text{-CH}_3\text{OC}_6\text{H}_4\text{=CK}$ (II) with the methyl ester
of 2-ethyl-3-methylcyclohexanecarboxylic-3-acid (III)
in tertiary butanol (six hours at 90°C) resulted in the

Card 1/7

CZECHOSLOVAKIA/Organic Chemistry - Natural Compounds and Their
Synthetic Analogs.

G.

Abs Jour : Ref Zhur - Khimiya, No 16, 1958, 54013

formation of the lactone, 1-(m-methoxyphenyl-ethynyl)-2-ethyl-3-methyl-1-hydroxycyclohexancarboxylic-3-acid (V). A crude yield of 76% was obtained after chromatographic treatment on Al_2O_3 , b. p. 190-205°C/0.3 mm. The hydrogenation of V on Pd/C in methanol lead to the formation of the lactone, 1- β -(m-methoxyphenyl)-ethyl-2-ethyl-3-methyl-1-hydroxycyclohexancarboxylic-3-acid (IV), which was purified by chromatographic treatment with Al_2O_3 , b. p. 200-215°C/0.8 mm, 190-205°C/0.2 mm, m. p. 70°C. (from petroleum ether - benzene). Compound IV was also obtained by direct hydrogenation of the condensation product of III with II (without the intermediate separation of V), yield, 20.4%. The saponification of V with a 20% methanol KOH solution (boiling for 20 hours) produced 1- β -(m-methoxyphenyl)-ethyl-2-ethyl-3-methyl-1-hydroxycyclohexane carboxylic-3-acid,

Card 2/7

15

CZECHOSLOVAKIA/Organic Chemistry - Natural Compounds and Their
Synthetic Analogs.

G.

Abs Jour : Ref Zhur - Khimiya, No 16, 1958, 54013

m.p. 103-106°C (from petroleum ether - benzene).
The reduction of IV with lithium aluminum hydride re-
sulted in the formation of 1- $\sqrt[3]{\text{S}}$ -(m-methoxyphenyl)-
ethyl-2-ethyl-3-methyl-3-hydroxy-methyl cyclohexanol
(VI) in a 75% yield, b. p. 210-220°C./1.5 mm, m. p. 85-
87°C. (from petroleum ether). The cyclization of IV
was accomplished with aluminum chloride in C₆H₆ (boi-
ling for one hour while purging with dry HCl), followed
by methylation with dimethyl sulfate and then with
CH₃N₂, with the formation of the methyl ester of 1-ethyl-
2-methyl-7-methoxy-1, 2,3,4,9,10,11,12-octahydrophenan-
threne carboxylic-2-acid (VII), VIII acid), yield 58%,
b. p. 190°C./0.08 mm. The saponification of this pro-
duct with aqueous - alcoholic KOH solution at 180-190°C.
resulted in the formation of amorphous VIII, yield 5.6
grams (from 6.1 grams of VII);

Card 3/7

CZECHOSLOVAKIA/Organic Chemistry - Natural Compounds and Their
Synthetic Analogs.

G.

Abs Jour : Ref Zhur - Khimiya, No 16, 1958, 54013

Na-salt, m. p. 315-325°C. VIII melted at 50-60°C.,
resolidified and then melted again at 180-182°C.
A melting point of 189-191°C was obtained after recrystallization from methanol.

VIII possessed physiological activity and had IR spectra and a melting point identical with those of the C α -isomer of 7-methyldeisynolic acid, which has been synthesized before (Anner, G., Miescher K., Helv. chim. acta, 1947, 31, 1422), and probably possesses the cis-anti cis-configuration. The demethylation of VIII by heating with pyridine hydrochloride (4.5 hours at 170-190°C), resulted in the formation of I, yield 35%, m. p. 113-117°C. (from methanol). The condensation of the ethyl ester of 2-ketocyclohexyl acetic acid (b. p. 130-132°C./12 mm; 2,4-dinitrophenyl-hydrazone, m. p. 125-126°C. (from alcohol)),

Card 4/7

16

CZECHOSLOVAKIA/Organic Chemistry - Natural Compounds and Their
Synthetic Analogs.

G.

Abs Jour : Ref Zhur - Khimiya, No 16, 1958, 54013

with $C_6H_5C\equiv CK$ in tertiary butanol (5 hours at $\sim 200^\circ C$.) resulted in the formation of the lactone, 2-phenylethynyl-2-hydroxy cyclohexylacetic acid (yield 25%, b. p. $185-195^\circ C./1.6$ mm., m. p. $116-118^\circ C$. (from petroleum ether)), which upon hydrogenation with Pd/C in alcohol was transformed into the lactone, 2-(β -phenylethyl)-2-hydroxycyclohexyl acetic acid (IX acid) (yield 77%, b. p. $180^\circ C./0.9$ mm.), which is saponifiable with 10% methanol solution of KOH in IX, yield 78%, m. p. $118^\circ C$. (from benzene - petroleum ether). Upon heating 1.5 grams of IX with 30 ml of 90% H_3PO_4 (45 minutes at $110-120^\circ C$.) there was formed 1,2,3,4,9,10,11,12-octahydro-phenanthryl-1-acetic acid, yield 1.2 grams, m. p. $142^\circ C$. (from petroleum ether - benzene). The ethyl ester of β -(2-keto cyclohexyl)-protionic acid (b. p. $140-145^\circ C./10$ mm), was simultaneously converted into the lactone,

Card 5/7

CZECHOSLOVAKIA/Organic Chemistry - Natural Compounds and Their
Synthetic Analogs.

G.

Abs Jour : Ref Zhur - Khimiya, No 16, 1958, 54013

β -(2-phenyl ethynyl-2-hydroxycyclohexyl)-propionic acid (yield 51%, b. p. 180-230°C./1-5 mm, m. p. 83-84°C. (from petroleum ether), which product upon hydrogenation was converted into the lactone, β -(2- β -phenylethyl)-2-hydroxycyclohexyl)-propionic acid, yield 66%, m. p. 98°C. (from petroleum ether). Similarly, III was converted into the lactone of 1-phenylethynyl-2-ethyl-3-methyl-1-hydroxy cyclohexylcarboxylic-3 acid (yield 37%, b. p. 160-180°C./0.9 mm, m. p. 90°C. (from petroleum ether), which after hydrogenation over Pd/C, was converted into the lactone, 1-(β -phenylethyl)-2-ethyl-3-methyl-1-hydroxy cyclohexylcarboxylic-3 acid, m. p. 175-180°C./0.2 mm. II was synthesized from the ethyl ester of β -(m-methoxyphenyl)- α - β -dibromopropionic acid, m. p. 58-59°C. (from petroleum ether), prepared quantitatively by bromination of the ethyl

Card 6/7

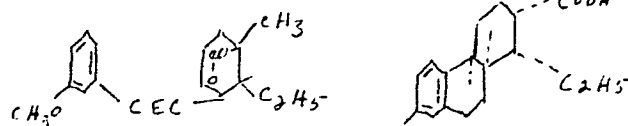
17

CZECHOSLOVAKIA/Organic Chemistry - Natural Compounds and Their
Synthetic Analogs.

G.

Abs Jour : Ref Zhur - Khimiya, No 16, 1958, 54013

ester of m-methoxy cinnamic acid. The curves of the
IR spectra of IV and VIII are furnished.
Communication XIV, see R. Zhur. Khim., 1958, 11219.



VIII.

Card 7/7

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khim., No 13, 1958, 43415.

Author : Borovicka Milos, Protiva Miroslav.

Inst :

Title : Antihistaminic Agents. XLI. Derivatives of 1-Aza-
2,3-5,6-Dibenzocycloheptadiene (Homoacridan)

Orig Pub: Chem. listy, 1957, 51, No 7, 1344-1349.

Abstract: To study their antihistaminic action a number of N-substituted derivatives of homoacridan (I) were synthesized; the HCl-salts of some I showed high activity; methiodides of I are less active. I, R = H (Ia), was prepared by reduction of lactam of 2'-amino-benzophenone-2-carboxylic acid with LiAlH₄ in ether (boiled for 5 hours), yield 73%, MP 131-132°C;

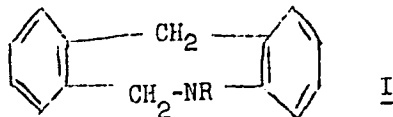
Card : 1/4

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry.

G-2

Abs Jour: Ref Zhur-Khim., No 13, 1958, 43415.

hydrochloride, MP 188-190°. Derivatives were synthesized by boiling



Ia with the corresponding RX and Na-anide in toluene. The following I were prepared (listing R, yield in %, BP in °C/mm, MP in °C of hydrochloride, its anti-histaminic activity in relation to benadryl, MP in °C of methiodide): (CH₃)₂NCH₂CH₂, 63, 150-154/0.5, 198-200, 10, 221-222, picrate, MP 171-172°; (C₂H₅)₂

Card : 2/4

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khim., No 13, 1958, 43415.

NCH_2CH_2 , 63, 175/0.9, 162-164 (dihydrochloride), 3, 209-210; $\text{CH}_2\text{CH}_2\text{N}(\text{CH}_2)_5$ -cyclo, 63, 180-185/0.5, 207-209 (dihydrochloride), 0.3, 200-201; $\text{CH}_2\text{CH}_2\text{N}(\text{CH}_2)_2\text{O}(\text{CH}_2)_4$, 62, 192-194/0.5 (MP 90-92°), forms no hydrochloride, —, 225; I, R = $\text{CH}_2\text{CH}(\text{CH}_3)\text{N}(\text{CH}_2)_2$, 57, 153/0.4, forms no hydrochloride, —, 207-209 (on preparation of methiodide there is formed as a by-product the methiodide of I, R = CH, MP 174-175°), picrate, MP 157-158°; $(\text{CH}_2)_4\text{NCH}_2\text{CH}_2\text{CH}_2$, 65, 180/0.4, 182-183, 800, 189-190. By boiling for 5 hours Ia with $\text{ClCH}_2\text{CH}_2\text{COCl}$ in C_6H_6 was prepared I, R = $\text{ClCH}_2\text{CH}_2\text{CO}$ yield 63%, MP 77-79°, which formed with $(\text{C}_2\text{H}_5)_2\text{NH}$ in toluene (boiling for 10 hours) the I, R = $(\text{C}_2\text{H}_5)_2\text{NCH}_2\text{CH}_2\text{CO}$ (BP 181-186°/0.35 mm), and with

Card : 3/4

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry.

G-2

Abs Jour: Ref Zhur-Khim., No 13, 1958, 43415.

CH_3SNa (boiling for 20 hours in acetone) the I, R
= $\text{CH}_3\text{SCH}_2\text{CH}_2\text{CO}$, BP $204-206^\circ/0.4$ mm; methiodide,
MP $123-125^\circ$. Methiodide of $(\text{CH}_3)_2\text{N}-(\text{CH}_2)_3\text{Cl}$ was
prepared, MP $210-212^\circ$.

Card : 4/4

CZECHOSLOVAKIA / Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khimiya, 23, 1958, 77702.

Author : Hach, V. and Protiva, M.

Inst : Not given.

Title : Antihistamines. XLII. Synthesis of 1-aza-4-thia-2,3-5,6-dibenzocycloheptadiene (homophenothiazine).

Orig:Pub: Chem Listy, 51, No 10, 1909-1914 (1957) (in Czech).

Abstract: When the methyl ester of thiosalicylic acid is added to a solution of CH_3ONa in CH_3OH and the mixture is heated for 15 hrs with o- NO_2 $\text{C}_6\text{H}_4\text{Cl}$ (50°), the methyl ester of 2'-nitrodiphenylsulfo-dicarboxylic-2 acid (I) is obtained, yield 55%, mp 92-93 $^\circ$. The reduction of a methanolic solution of I over Pt (from PtO_2) or over Raney nickel

Card 1/4

CZECHOSLOVAKIA / Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khimiya, No 23, 1958, 77702.

Abstract: at normal pressures gives the methyl ester of 2'-aminodiphenylsulfonic-2-carboxylic acid (II), yield 100%, mp 95-96° (from 75% alc); picrate (P) mp 167° (from alc). Heating II for 7 hrs at 200-220° gives the lactam of II (III), yield 86%, mp 239-242° (evap; from aqueous alc). The reduction of III by refluxing for 30 hrs with LiAlH₄ in ether gives 1-aza-4-thia-2,3:5,6-dibenzocycloheptadiene (homophenothiazine) (IV), mp 115° (from alc). Refluxing IV for 10 hrs with NaNH₂ and ClCH₂ CH₂ N(CH₃)₂ in xylene gives N-(2-dimethyl-aminoethyl)-IV (V), yield 5% bp 160-165°/0.5mm; hydrochloride mp 206° (from ether-alc); P mp 156° (from alc); iodomethylate (IM) mp 195° (from ether-

Card 2/4

CZECHOSLOVAKIA / Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khimiya, No 23, 1958, 77702.

Abstract: alc). Using a procedure similar to that used in the preparation of V, N-(2-piperidinoethyl)-IV (VI) is obtained from IV and $\text{ClCH}_2\text{CH}_2\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2$, bp $180^\circ/0.5\text{mm}$; acid salt of succinic acid mp $150-151^\circ$ (from alc); P mp 165° (from alc). Similarly IV and 1-dimethylamino-2-chloropropane give N-(2-dimethylaminopropyl)-IV, yield 68%, bp $165-170^\circ/0.5\text{mm}$; P mp 158° (from alc); IV and 1-dimethylamino-3-chloropropane give N-(3-dimethylaminopropyl)-IV, yield 67%, bp $169-173^\circ/0.5\text{mm}$; hydrobromide mp 157° (from ether-alc); P mp 135° (from alc). Heating of IV for 3 hrs with ClCH_2COCl in C_6H_6 at 80° gives N-(chloroacetyl)-IV (VII), yield 78%, mp 103° (from alc);

Card 3/4

CZECHOSLOVAKIA / Organic Chemistry. Synthetic Organic Chemistry. G-2

Abs Jour: Ref Zhur-Khimiya, No 23, 1958, 77702.

Abstract: similarly IV and $\text{ClCH}_2\text{CH}_2\text{COCl}$ give N-(β -chloropropionyl)-IV (VIII), yield 48%, mp 98° (from alc). The refluxing of VII with $(\text{C}_2\text{H}_5)_2\text{NH}$ in C_6H_6 for 16 hrs gives N-diethylaminoacetyl)-IV, yield 76%, bp 190-195°/0.6mm, mp 51-53° (from petroleum ether); P mp 175° (from alc); bromoethylate mp 188° (decomp; from ether-alc). Refluxing of VIII for 6 hrs with dry CH_3SNa in acetone gives N-(β -methylmercaptopropionyl)-IV, bp 175-180°/0.8mm; IM mp 133° (decomp). V possesses high histaminic activity while VI is a local anesthetic. For Communication XVI see RZhKhim, 1958, 43415. -- A. Emr.

Card 4/4

CZECHOSLOVAKIA / Organic Chemistry. Natural Substances and Their Synthetic Analogues. G

Abs Jour: Ref Zhur-Khimiya, No 18, 1958, 61101.

Author : Miroslav Protiva, Jiri Jilek, Erika Hachova,
Ludvik Novak, Zdenek J. Vejdelek, Edita Adlerova.
Inst : Chemical Society (U.S.A.).
Title : Synthetic Models of Blood Pressure Decreasing
Alkaloids. I. 1-Aralkyl-1,2,3,4-Tetrahydronorharmans.

Orig Pub: Chem. listy, 1957, 51, No 10, 1915-1922.

Abstract: The 1-aralkyl-1,2,3,4-tetrahydronorharmans described in the paper are depicted by the general structural formula A and characterized by a hypotensive action similar to the action of reserpine. Triptamine (I) is prepared by the reduction of 3-indolylacetonitril by the action of Na in alcohol,

Card 1/11

CZECHOSLOVAKIA / Organic Chemistry. Natural Substances and Their Synthetic Analogues. G

Abs Jour: Ref Zhur-Khimiya, No 18, 1958, 61101.

Abstract: or by Radney's catalyst under pressure, or with LiAlH_4 , yield 52 to 56%, boiling point $158^\circ/0.5$ mm, melting point 112 to 113° (from benzene). 5-methoxytryptamine, melting point 120 to 121° , and 7-methoxytryptamine, melting point 134 to 135° , are prepared according to Spath and Lederer (Spath E., Lederer E., Ber., 1930, 63, 2102). $(\text{CH}_3)_2\text{C}(\text{C}_6\text{H}_5)\text{CONH}$, melting point 160° , is prepared by hydrolyzing $(\text{CH}_3)_2\text{C}(\text{C}_6\text{H}_5)\text{CN}$ with aqueous KOH, it produces $(\text{CH}_3)_2\text{C}(\text{C}_6\text{H}_5)\text{COOH}$, melting point 77° , at the continued hydrolysis in KOH. Hydrochloride

Card 2/11

CZECHOSLOVAKIA / Organic Chemistry. Natural Substances G
and Their Synthetic Analogues.

Abs Jour: Ref Zhur-Khimiya, No 18, 1958, 61101.

Abstract: (II) of that acid is prepared thereof by the action of SOCl_2 , yield 90%, boiling point $109^\circ/16$ mm. The following is prepared neutralizing the benzene solution of a corresponding triptamine with the benzene solution of a corresponding acid as, for example, phenylacetic acid (PNA), boiling and cooling; 7-methoxytriptamine salt of PNA (III), melting point 190° ; 5-methoxytroptamine salt of PNA (IV), melting point 160° ; triptamine sale of diphenylacetic acid, melting point 193.5 to 194.5° ; and triptamine salt of PNA (V), melting point 178 to 179° . The following triptamines are prepared by: a/ 1hour's heating of the corresponding triptamine salt above its melting point, b/ heating the equimolar mixture of corresponding I with the

Card 3/11

CZECHOSLOVAKIA / Organic Chemistry. Natural Substances G
and Their Synthetic Analogues.

Abs Jour: Ref Zhur-Khimiya, No 18, 1958, 61101.

Abstract: corresponding acid, and c/ of the corresponding I
and hydrochloride of the corresponding acid in
 C_6H_6 in the presence of aqueous NaOH at about 20° .
5-methoxytryptamine of PNA (VI), melting point
 117° (from CH_3OH), was prepared of IV according
to the method a, yielded 80%. Triptamide of 4-
methoxy-PNA (VII), melting point 155 to 156° (CH_3
OH), was prepared of I and methoxy-PNA by the
method b, yield 46%. Triptamide of α -phenyliso-
butyric acid (VIII), melting point 137 to 138°
(from benzene), was prepared of I and IV by the
method c, yield 91%. Triptamide of PNA (IX), melt-

Card 4/11

CZECHOSLOVAKIA / Organic Chemistry. Natural Substances G
and Their Synthetic Analogues.

Abs Jour: Ref Zhur-Khimiya, No 18, 1958, 61101.

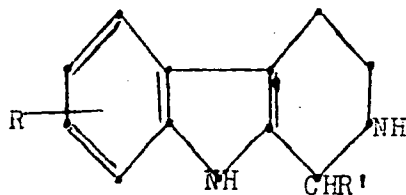
Abstract: ing point 145 to 146° (from CH₃OH), was prepared of V by the method a, yield 72%, or of I by the method b (46%). Triptamide of β -phenylpropionic acid (X), melting point 72 to 73° (from aqueous CH₃OH), was prepared of I by the method c, yield 30%. Triptamide of γ -phenylbutyric acid (XI), melting point 112 to 113° (from benzene), was synthesized of I by the method b, yield 45%. Triptamide of diphenylacetic acid, melting point 145° (from CH₃OH), was prepared of I by the method c, yield 90%, or by the method b. The cyclization of that triptamide into the corresponding 3,4-dihydronorharman did not succeed. Triptamide of 1-naphthylacetic acid (XII), melting point 157 to 158° (CH₃OH), was prepared of I by the method b,

Card 5/11

CZECHOSLOVAKIA / Organic Chemistry. Natural Substances G
and Their Synthetic Analogues.

Abs Jour: Ref Zhur-Khimiya, No 18, 1958, 61101.

Abstract:



yield 79%. 7-methoxytryptamide of PNA (XIII),
melting point 101 to 102° (from aqueous CH₃OH),

Card 6/11

CZECHOSLOVAKIA / Organic Chemistry. Natural Substances and Their Synthetic Analogues. 3

Abs Jour: Ref Zhur-Khimiya, No 18, 1958, 61101.

Abstract: was prepared of III by the method a, yield 60%. 1-(2-phenylethyl)-3,4-dihydronorharman (XIV) is prepared by boiling X 1 hour with POCl_3 in C_6H_6 ; picrate - melting point 189° (from CH_3OH). Unpurified XIV (a.6 g) is reduced with 10 g. of Na in 120 ml of alcohol into 1-(2-phenylethyl)-1,2,3,4-tetrahydronorharman (XV), yield 1.7 g, melting point 75° (from CH_3OH); hydrochloride - melting point 258 to 259° (from CH_3OH); methanesulfonate (MS) - melting point 242 to 243° . Same as XIV, 6 g of unpurified 1-(3-phenylpropyl)-3,4-dihydronorharman (XVI) is obtained from 5 g of XI; picrate - melting point 164 to 165° (from CH_3OH). XVI reduced in the same way as in the case of XV produced 1-(3-phenylpropyl)-1,2,3,4-tetrahydronor-

Card 7/11

62

CZECHOSLOVAKIA / Organic Chemistry. Natural Substances G
and Their Synthetic Analogues.

Abs Jour: Ref Zhur-Khimiya, No 18, 1958, 61101.

Abstract: harman; MS - melting point 245 to 247°. Other 1,2,3,4-tetrahydronorharmans of the general formula A are prepared (if not indicated otherwise) by the cyclisation of the corresponding triptamide (same as XIV) and reduction of the produced raw 3,4-dihydronorharman (same as XV): A, R = H, R' = $\text{C}_6\text{H}_5\text{C}(\text{CH}_3)_2$ -, (from VIII), MS - melting point 225 to 226°; R = H, R' = 5,6,7,8-tetrahydro-1-naphthylmethyl, (from XIII), hydrochloride - melting point 247 to 253° (from aqueous alcohol), MS - melting point 239 to 241°; R = 6-OCH₃, R' = $\text{C}_6\text{H}_5\text{CH}_2$ -, (from VI), MS - melting point 249°;

Card 8/11

CZECHOSLOVAKIA / Organic Chemistry. Natural Substances G
and Their Synthetic Analogues.

Abs Jour: Ref Zhur-Khimiya, No 18, 1958, 61101.

Abstract: R = 8-OCH₃, R' = C₆H₅CH₂, (from XIII), MS - melting point 249 to 250°; R = H, R' = 4-OCH₃C₆H₄CH₂, (from VII) or by aging 24 g of I hydrochloride with 24 g of 4-CH₃OC₆H₄CH₂COCOOH in 600 ml of water and 360 ml of acetic buffer (pH = 3.8) in the duration of 40 days at 37°, decarboxylation of the formed 1-(4-methoxybenzyl)-1,2,3,4-tetrahydronorharman-1-carboxylic acid (melting point of raw acid 223 to 225°; dissociates), passing HCl (gas) through its suspension in boiling CH₃OH, dissolution of the raw product in CHCl₃ and filtration through Al₂O₃; hydrochloride - melting point 252 to 254° (from CH₃OH); MS - melting point 252 to 253°; A, R = H, R' = C₆H₅, melting point

Card 9/11

63

CZECHOSLOVAKIA / Organic Chemistry. Natural Substances G
and Their Synthetic Analogues.

Abs Jour: Ref Zhur-Khimiya, No 18, 1958, 61101.

Abstract: 157 to 159⁰, by cyclization of benzaltriptamine
(Hoshino T., Kotake J., Liebigs Ann. Chem., 1935,
516, 76); hydrochloride - melting point 258 to
260⁰, MS - melting point - 250 to 251⁰; R = H,
R' = C₆H₅CH₂ (XVII), (from IX or from I hydro-
chloride and C₆H₅CH₂CHO (Hahn G., Ludewig H., Ber.,
1934, 67, 2031), MS - melting point 258 to 260⁰;
R = H, R' = 3,4-(CH₃O)₂C₆H₃CH (from I hydrochlor-
ide and 3,4-(CH₃O)₂C₆H₃CH₂CO₂COOH) (RZhKhim, 1956,
58170), MS - melting point 236-238⁰. 1-benzyl-
norharman is prepared of XVII by dehydrogenation
(Clemo G. R., Swan G. A., J. Chem. Soc., 1946,

Card 10/11

CZECHOSLOVAKIA / Organic Chemistry. Natural Substances G
and Their Synthetic Analogues.

Abs Jour: Ref Zhur-Khimiya, No 18, 1958, 61101.

Abstract: 621); MS - melting point 210 to 211° (from alcohol-acetone).

Card 11/11

64

PROTIVA, M

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64393.

Author : Hach Vladimir, Protiva Miroslav

Inst :

Title : Synthetic Research in the Area of Estrogenic Hormones.
XVI. Synthesis of Hydrindandione - 1.4

Orig Pub: Chem. listy, 1957, 51, No 11, 2099-2108.

Abstract: Hydrindandione-1.4 (I) is synthesized from o-nitrohydrocinnamic acid (II) by the following manner. The cyclization of acid chloride II with the application of $AlCl_3$ in CS_2 leads to 4-nitroindanone (III), yield 62%, melting point 103° (from petroleum ether or alcohol): oxime, melting point 204° (from alcohol). During hydrogenation of III over PtO_2 or over skeleton Ni in alcohol, 4-amino-indanone is formed, yield in the latter case

Card : 1/8

10

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64393.

95%, melting point 123-124° (from bz1.), monodiazotization and subsequent heating (15 minutes at 40°) lead to 4-oxyindanone (IV), yield 83%, melting point 240° (from aqueous alcohol); oxime (V), melting point 186° (from aqueous alcohol) IV is also synthesized from dehydrocoumarin by a method described (RZhKhim, 1955, 37283), yield 42%. During hydrogenation of V over Pt (from PtO₂) in CH₃COOH, there is formed 1-amino-cis-hydrindan [yield 21.3%, boiling point 60-62°/0.5 mm; picrate, melting point 182-184° (from alcohol); N-benzoyl derivative, melting point 182-183° (from 50% alcohol)] and 1-amino-cis(?) -hydrindanol (VI) [yield 32%, boiling point 122-125°/0.5 mm, melting point 75-77° (from petroleum ether)]. Monodiazotization of VI in 25% CH₃COOH and subsequent heating (2.5 hours in

Card : 2/8

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64393.

a water bath) leads into hydrindandiol-1.4 (yield 25%, boiling point 122-126°/0.5 mm), which during oxidation by the chrome mixture in aqueous CH_3COOH transfers in I, yield 61%; Big-2,4-dinitrophenylhydrazine, melting point 220-223° (from bz1-petroleum ether). The cyclization of o-methoxyhydrocinnamic acid (VII) and o-isopropoxyhydrocinnamic acid (VIII) (under the action of polyphosphoric acid, P_2O_5 in bz1, H_2SO_4 or POCl_3 in CCl_4 or xylene) in 4-methoxyindanone and accordingly in 4-isopropoxyindanone from which it would be possible to obtain I, was not successful. II is synthesized by three ways: a) by boiling (24 hours) of β -(o-nitrophenyl)-propionic acid, which after boiling with the solution H_2SO_4 (1 hour) was transferred into II, 40% yield (unpurified); b) from o- $\text{NO}_2\text{C}_6\text{H}_4\text{CH}_2\text{Cl}$ and malonic acid by

Card : 3/8

//

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64393.

a method described (Janisch A., Ber., 1923, 56, 2448), yield 24%; c) by nitrating of the hydrocinnamic acid by a method described (Konek F.V., Pacsu E., Ber., 1918, 51, 855) with a subsequent division of II and n-nitrohydrocinnamic acid (IX), melting point 164°. Chlorohydrid II during condensation with C_6H_6 in the presence of $AlCl_3$ (4 hour boiling) forms β -(o-nitrophenyl)-propiophenone, yield 40%, melting point 67-68° (from alcohol); analogous condensation of chlorohydrid of IX leads to β -(n-nitrophenyl)-propiophenone, yield 76%, melting point 92-93° (from alcohol). VII is obtained in the following manner. Condensation of $o-CH_3OC_6H_4CHO$ with $CNCH_2COOC_2H_5$ in alcohol in the presence of piperidine leads to ethyl ether of α -cyan-o-methoxycinnamic acid

Card : 4/8

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64393.

[yield 71.5%, melting point 74° (from alcohol)], which during hydrogenation over Pt (from PtO₂) in alcohol ethyl ether forms α-cyan-β-(o-methoxyphenyl)-propionic acid (X), and during boiling (16 hours) with aqueous CH₃COOH-H₂SO₄ gives o-methoxycinnamic acid (XI), yield 51%, melting point 182° (from water). X is obtained also with 90% yield from O-CH₃CC₂H₄CHO and malonic ether in C₂H₅N in the presence of piperidine. Boiling of X with aqueous H₂SO₄ (8 hours) or reduction of XI by an amalgam of Na lead to VII, yield 72.5 and 80%, melting point 90-91° (from water). For obtaining VIII by boiling (30 hours) of salicyl aldehyde with iso-C₃H₇Br in the presence of C₂H₅ONa and KI, o-isopropoxy-benzaldehyde (yield 27%, boiling point 72-73°/0.3 mm)

Card : 5/8

12

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64393.

is synthesized, which with malonic ether in C_5H_5N in the presence of piperidine give o-isopropoxycinnamic acid [yield 64%, melting point 125° (from 30% alcohol)] reduced by an amalgam of Na to VIII, yield 78%, boiling point 135-140°/0.3 mm, melting point 51°/(from water). The following transformations were also realized. The reduction of VII $LiAlH_4$ leads to 3-(o-methoxyphenyl)-propanol (yield 60%, boiling point 117-120°/0.5 mm), which with PBr_3 gives 3-(o-methoxyphenyl)-propylbromide, yield 58%, boiling point 85-89°/0.5 mm; the latter with KCN forms 3-(o-methoxyphenyl)-butyronitrile (yield 74%, boiling point 145-155°/12-14 mm), converted by saponification into 3-(o-methoxyphenyl)-butyric acid (yield 73%, boiling point 145-147°/0.3 mm, melting point 40°), which during cyclization under the action

Card : 6/8

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour; Ref. Zhur-Khimiya, No 19, 1958, 64393.

of POCl_3 in CCl_4 was transformed into 5-methoxytetralone (XII), yield 52%, melting point $88-89^\circ$. The action of SO_2Cl_2 on XII (10 minutes, at temperature of 20°) leads to 2,2-dichlor-5-methoxytetralone, melting point 100° (from petroleum ether) and the processing of XII Br_2 into CH_3COOH (one hour at temperature 20°) leads to 2-brom-5-methoxytetralone, melting point 93° (from petroleum ether). The action of SO_2Cl_2 on decalindione-1.5 leads to dichloride, which is 2,2-dichlordecalindione-1.5 or 2,6-dichlordecalindione-1.5, yield 37%, melting point $153-154^\circ$ (from bzl. petroleum ether). By the interaction of 2-acetoxycyclohexanone with diethyloxalate in C_6H_6 in the presence of dry $\text{C}_2\text{H}_5\text{ONa}$ (7 hours, at a tempera-

Card : 7/8

13

CZECHOSLOVAKIA/Organic Chemistry. Synthetic Organic Chemistry. G

Abs Jour: Ref. Zhur-Khimiya, No 19, 1958, 64393.

ture $\sim 20^\circ$) there is obtained, with a low yield, 2-carbethoxy-6-acetoxycyclohexanone, boiling point $80-83^\circ/0.35$ mm. Analogously from 2-methoxycyclohexanone is synthesized 2-carbethoxy-6-methoxycyclohexanone, boiling point $125-130^\circ/10$ mm. Report XV, see RZhKhim, 1958, 54013.

Card : 8/8

CZECHOSLOVAKIA/Organic Chemistry. Natural Substances and
Their Synthetic Analogues.

G

Abs Jour: Ref Zhur-Khimiya, No 22, 1958, 74167.

Author : Miroslav Protiva, Jiri O. Jilek. Vladimir Hach,
Edita Adlerova, Vladimir Mychajlyszyn.

Inst : American Chemical Society.

Title : Synthetic Models of Blood Pressure Depressing Alkaloids.
II. Simple Models of Reserpine With Cyclohexane Ring.

Orig Pub: Chem. listy, 1957, 51, No 11, 2109-2117.

Abstract: Cyclohexylacetic acid (I) was prepared by the re-
duction of a solution of sodium cyclohexylidene-
acetate on Raney nickel under 110 atm. at 100°,
yield 86%, boil p. 123 to 125°/5 mm; it was con-
verted into cyclohexylacetylchloride (II) by the

Card : 1/11

CZECHOSLOVAKIA/Organic Chemistry. Natural Substances and
Their Synthetic Analogues.

G

Abs Jour: Ref Zhur-Khimiya, No 22, 1958, 74167.

action of SOCl_2 , yield 92%, boil. p. 85 to 88°/
20 mm. The tryptamine salt of I was synthesized
of tryptamine (III) and I, yield 88%, melt. p.
181 to 182° (from alc.), and converted into trypta-
mid of I (IV) by heating it 45 min. to 190 to 200°,
little yield, melt. p. 79 to 81° (from benzene).
IV was obtained with a considerably greater yield
(85%) of III and II by cooling them in C_6H_6 in the
presence of 4%-ual aqueous NaOH solution. A solid
impure dihydro base was prepared by boiling 3.9 g
of IV with 10 ml of POCl_3 in 100 ml of C_6H_6 in
the duration of 2 hours, evaporating in vacuo, dis-
solution in 60 ml of 75%-ual CH_3COOH , and precipita-

Card : 2/11

CZECHOSLOVAKIA/Organic Chemistry. Natural Substances and
Their Synthetic Analogues.

G

Abs Jour: Ref Zhur-Khimiya, No 22, 1958, 74167.

tion by NH_4OH ; that base was reduced with 12 g of Na in 120 ml of alcohol to 1-cyclohexylmethyl-1,2,3,4-tetrahydronorharman (V) (yield 3.6 g); hydrochloride, melt. p. 245 to 246° (from alc.); metasulfonate, melt. p. 262 to 265° (from aqu. alc.). Ethyl ester (EE) of 1-oxy-4-methoxycyclohexylacetic acid was synthesized of 4-methoxycyclohexanone (VI) and $\text{CH}_2\text{Br}-\text{COOC}_2\text{H}_5$ in C_6H_6 by the reaction of Reformatskiy, yield 64%, boil. p. 110 to 111°/1.6 mm; it produced the EE of 4-methoxycyclohexenylacetic acid (VII) after 4 hours of action of SOCl_2 in pyridine in an ice bath, boil. p. 120°/14 mm. 4-methoxycyclohexenylacetic acid (VIII) was prepared by 12 hour boiling of VII with

Card : 3/11

CZECHOSLOVAKIA/Organic Chemistry. Natural Substances and
Their Synthetic Analogues.

G

Abs Jour: Ref Zhur-Khimiya, No 22, 1958, 74167.

KOH solution in alcohol, yield 85%, boil. p. 150 to 152°/2 mm, melt. p. 27 to 30°. Hydrogenation of VII on PtO₂ in CH₃COOH resulted in EE of 4-methoxycyclohexylacetic acid (IX), boil. p. 120 to 122°/20 mm. By hydrogenation of the aqueous solution of Na salt of VIII on Raney's nickel under 105 atm. at 80 to 90°, or by 12 hour boiling of IX with KOH solution in alcohol, cis-(?)-4-methoxycyclohexylacetic acid was produced, yield 80%, boil. p. 151 to 152°/3 mm, melt. p. 19 to 22°; S-benzylisothiouronic salt, melt. p. 145 to 146° (from alc.). 4-methoxycyclohexylacetyl chloride, boil. p. 108 to 111°/10 mm, synthesized of the

Card : 4/11

CZECHOSLOVAKIA/Organic Chemistry. Natural Substances and
Their Synthetic Analogues.

G

Abs Jour: Ref Zhur-Khimiya, No 22, 1958, 74167.

above mentioned acid with a yield of 94% by 3 hours of seasoning and 1 hour of boiling with SOCl_2 was converted into tryptamide of 4-methoxycyclohexylacetic acid similarly to II by reducing with III, yield 56%, melt. p. 102° (from benzene); that tryptamide was cyclized similarly to IV to the corresponding dihydro base, by the reduction of which with Na in alcohol 1-(4-methoxy-cyclohexyl)-methyl-1,2,3,4-tetrahydronorharman (X) was prepared, yield 82%; hydrochloride, melt. p. 245 to 247° (dissociates, from aqu. alc.); methanesulfonate, melt. p. 254 to 255° (from aq. alc.). 4-methoxycyclohexenylacetone nitryl (XI), boil. p. 118 to $121^\circ/10$ mm, was prepared of VII and cyanacetic acid in C_6H_6 in the presence

Card : 5/11

CZECHOSLOVAKIA/Organic Chemistry. Natural Substances and
Their Synthetic Analogues.

G

Abs Jour: Ref Zhur-Khimiya, No 22, 1958, 74167.

of $\text{CH}_3\text{COONH}_4$ by 7 hour boiling with azeotropic water removal; XI was boiled 3 hours with 10%-ual NaOH and VIII was produced, yield 61%. 4-methoxycyclohexenylacetyl chloride (XII) produced of VIII and SOCl_2 was added drop by drop with simultaneous cooling to concentrated NH_4OH and 4-methoxycyclohexenylacetamide (XIII) was obtained, yield 45%, melt. p. 126° (from iso- $\text{C}_7\text{H}_7\text{OH}$). 1.5 g of 2-(4-methoxycyclohexenyl)-ethylamine hydrochloride (XIV) was prepared by adding the solution of 3 g of XI in 10 ml of ether drop by drop to 1 g of LiAlH_4 in 10 ml of ether at -5° , 30 min. seasoning at -5° , 2 hour boiling, decomposition with 5 ml of water and 20 ml of 40%-ual NaOH, extraction of the ether

Card : 6/11

CZECHOSLOVAKIA/Organic Chemistry. Natural Substances and
Their Synthetic Analogues.

G

Abs Jour: Ref Zhur-Khimiya, No 22, 1958, 74167.

solution with dilute HCl, and evaporation of the acid solution in vacuo, melt. p. 231 to 232° (from iso-C₇H₇OH + alc.); picrate, melt. p. 190° (from alc.). When the reaction mixture had been decomposed with water after the reduction of XI and the ether layer, dried with the application of K₂CO₃, had been distilled, a base (XV), boil. p. 104 to 106/10mm, was obtained, the hydrochloride of which is of the same composition as XIV, and the melt. p. is 162° (from acetone + alc. + eth.); picrate, melt. p. 148 to 149° (from alc.). It is surmised that a change of the position of the double bond takes place at the distillation of the base of XIV and that XV is 2-(4-methoxycyclohexylidene)-ethylamine. The esterification of the

Card : 7/11

CZECHOSLOVAKIA/Organic Chemistry. Natural Substances and
Their Synthetic Analogues.

G

Abs Jour: Ref Zhur-Khimiya, No 22, 1958, 74167.

β -methoxyadipinic acid in the mixture toluene-
alcohol in the presence of H_2SO_4 at a simultaneous
azeotropic removal of water leads to ethyl ester of
 β -methoxyadipinic acid, yield 80%, boil. p. 118
to 120°/2.5 mm, $n_D^{20} = 1.4336$. By the reduction
of EE of 4-oxyphenylacetic acid in alcohol on Raney's
nickel in the presence of C_2H_5ONa under 125 atm and
at 150 to 160°, EE of 4-oxy-cyclohexylacetic acid
was obtained, yield 61%, boil. p. 115 to 116°/0.4 mm,
which was saponified by 2 hour boiling with NaOH solu-
tion in aqueous alcohol to a mixture of stereoisomeric
4-oxy-cyclohexylacetic acids, yield 94%, melt. p. 110
to 120° (raw). 4-oxy-cyclohexylacetic acid was prepared

Card : 8/11

CZECHOSLOVAKIA/Organic Chemistry. Natural Substances and
Their Synthetic Analogues.

G

Abs Jour: Ref Zhur-Khimiya, No 22, 1958, 74167

by the oxidation of the above mentioned mixture
by seasoning it 3 days in $\text{Na}_2\text{Cr}_2\text{O}_7$ solution in
dilute H_2SO_4 , yield 28%, melt. p. 103 to 106°
(from petr. eth. + ethylacetate); semicarbazone,
melt. p. 185° (from water); ethyl ether 2,4-dinitro-
phenylhydrazone, melt. p. 150 to 152° (from alc.).
2-(4-methoxyphenyl)-ethylamine was methylated by
8 hours' heating with 98%-ual HCOOH and 37%-ual
 CH_3O to hordenine methyl ester (XVI), yield 37%,
boil. p. 122 to 125°/10 mm, hydrochloride, melt.
p. 173 to 174° (not adjusted). Hordenine (XVII)
was prepared of XVI by Buck's method (Buck J.S.
and others, J. Amer. Chem. Soc., 1938, 60, 1789),
yield 74%, melt. p. 117° (not adjusted); hydrochloride,

Card : 9/11

CZECHOSLOVAKIA/Organic Chemistry. Natural Substances and
Their Synthetic Analogues:

G

Abs Jour: Ref Zhur-Khimiya, No 22, 1958, 74167.

melt. p. 177° (from alc. + eth.). Hexahydrohorden-
ine (XVIII) was produced by hydrogenating XVII on
Pt from PtO₂ in CH₃COOH, yield 58%, boil. p. 132 to
134°/10 mm; 2-(cyclohexylethyl)-dimethyl-amine was
separated as a by-product of hydrogenation, yield 19%,
boil. p. 82 to 84°/10 mm; picrate, melt. p. 154°
(not adjusted, from alc.). 3,4,5-trimethoxybenzoate
of XVIII (XIX), semisolid if impure, was synthesized of
XVIII and 3,4,5-trimethoxybenzoylchloride by seasoning
(about 12 hours) in C₂H₄; hydrochloride, melt. p. 214°
(not adjusted, from alc. + eth.). V and X show a
hypotensive activity same as their aromatic analogues
described in the report I (see RZhKhim, 1958, 61101).
The substance XIX is not active. The position of the

Card : 10/11

CZECHOSLOVAKIA/Organic Chemistry. Natural Substances and
Their Synthetic Analogues.

G

Abs Jour: Ref Zhur-Khimiya, No 22, 1958, 74167.

double bond was not established in the case of
hexenyl compounds VII, VIII and XI to XIV; it is
assumed by analogy with bibliographical indications
that they are Δ^1 -compounds. The melting points
were determined in a Kofler block, and those denoted
"not adjusted" were determined with a capillary.

Card : 11/11

CZECHOSLOVAKIA / Organic Chemistry. Synthesis.

G-2

Abs Jour: Ref Zhur-Khimiya, No 3, 1959, 8246.

Author : Borovicka, Milos., Protiva, Miroslav.
Inst : Not given.
Title : Sympathic Ganglia-Blocking Substances.

Orig Pub: Chem. listy, 1957, 51, No 11, 2118-2121.

Abstract: For physiological tests were synthesized the substances $C_6H_5CH_2CH_2N(CH_3)_2$ (I) and $C_6H_5CH_2CH_2N(C_2H_5)_2$ (II) a - d, a R = CN, b $CONH_2$, c CH_2NH_2 , d H) and some of their derivatives were prepared. By a described method (Blicke F. F. et al., J. Amer. Chem. Soc., 1952, 74, 1844) Ia was prepared from $C_6H_5CH_2CN$ (III) and $(CH_3)_2NCH_2CH_2Cl$ in the presence of $NaNH_2$, yield 87%, BP $140^\circ/1.2$ mm; dipicrate, MP $238-239^\circ$ (from acetophenone-

Card 1/4

G-2

CZECHOSLOVAKIA / Organic Chemistry. Synthesis.

Abs Jour: Ref Zhur-Khimiya, No 3, 1959, 8246.

Abstract: alcohol); bis-methiodide (IV), MP 254-255°. In the same manner was prepared IIa, BP 140-142°/0.1 mm (purified by decomposition of dipicrate); dipicrate, MP 131-162° (from acetone-alcohol). On rapid addition of $(C_2H_5)_2NCH_2CH_2Cl$ to mixture of III and $NaNH_2$ in C_6H_6 there is formed as a result of a vigorous reaction, together with IIa also IIId, BP 128-135°/0.6 mm; dipicrate, MP 124-126° (from acetone-alcohol); bis-methiodide (V), MP 190-192° (dried at 100°). Oily hydrochloride synthesized by addition of an excess of 10% solution of HCl-gas in ether to 10 g of Ia in ether, is dried in vacuum and heated for 20 minutes at 80-95° with 50 ml of concentrated H_2SO_4 and 1.2 ml water. Yield of Ib 53%, BP 140-165°/0.4 mm.

Card 2/4

84

CZECHOSLOVAKIA / Organic Chemistry. Synthesis.

G-2

Abs Jour: Ref Zhur-Khimiya, No 3, 1959, 8246.

Abstract: MP 103-104° (from benzeno-petroleum ether); bis-methiodide (VI), MP 257-259° (from methyl alcohol-ether). Analogously was prepared IIb, yield 51%, MP 86-88° (from ether-petroleum ether); dipicrate, MP 183-184° (from acetophenone-alcohol); bis-methiodide (VII), MP 190-192°, softening point 161-162° (from alcohol-acetone-ether). Reduction of Ia over skeleton Ni (100°, initial pressure 105 atmospheres CH₃OH, saturated with NH₃ while cooling) gave Ic, yield 66%, BP 118-120°/0.4 mm. On crystallization of crude picrate of Ic from acetophenone-ether mixture (5:2) there is formed the dipicrate of 3-phenyl-3-(alpha-methylbenzylideneamino)-methyl-1,5-bis-dimethylaminopentane, MP 163-164°. 2.6 g Ic, 0.8 g NaOH in 10 ml alcohol are boiled for 10 hours with 7.1 g

Card 3/4

CZECHOSLOVAKIA / Organic Chemistry. Synthesis.

G-2

Abs Jour: Ref Zhur-Khimiya, No 3, 1959, 8246.

Abstract: CH_3I , added 7.1 g CH_3I and 10 ml acetone, boiled 1 hour, and isolate 3.2 g of monohydrate of tris-methiodide of 3-phenyl-3dimethylaminoethyl-1,5-bis-diethylamino-pentane (VIII), $\text{MP } 153-154^\circ$ (decomposes; CH_3OH -ether). Analogously to Ic was prepared IIc, yield 76%, BP $145-147^\circ/0.4$ mm; tripicrate, $\text{MP } 187-189^\circ$ (from acetophenone-alcohol). Boiling of IIc with $(\text{CH}_3\text{CO})_2\text{O}$ in toluene (15 minutes) gives acetate of IIc, BP $180-190^\circ/1.4$ mm; dipicrate, $\text{MP } 131-133^\circ$ (from acetone-alcohol); bis-methiodide (IX), $2\text{C}_{24}\text{H}_{45}\text{ON}_3\text{I}_2 \cdot \text{C}_3\text{H}_6\text{O} \cdot \text{CH}_4\text{O}$ (from acetone- CH_3OH -ether), $\text{MP } 143^\circ$. IV-IX show very slight ganglionic-blocking action. Communication V see RZhKhimBkh, 1958, 31557. -- Antonin Emr.

Card 4/4

85

Protiva, M.
CZECHOSLOVAKIA / Organic Chemistry--Synthetic organic chemistry. C-2

Abs Jour : Ref Zhur - Khimiya, No 14, 1959, No. 49483

Author : Protiva, M.; Exner, O.; Borovicka, M.

Inst : Not given

Title : Antihistamine Compounds. XLIII. Derivatives of
Diphenylhydramine with Polar Substituents

Orig Pub : Ceskoslov Farmac, 7, No 7, 380-385 (1958)

Abstract : Continuing their work on the synthesis of antihistamine compounds, the authors have apparently synthesized
4-HOC₆H₄CH(C₆H₅)OCH₂CH₂N(CH₃)₂ (I) by the reaction of
4-CH₃COOC₆H₄CH(OH)C₆H₅ (II) with ClCH₂CH₂N(CH₃)₂ (III).
The isomer of I, 4-(CH₃)₂NCH₂CH₂OC₆H₄CH(OH)C₆H₅ (IV) has
been synthesized by the scheme: 4-HOC₆H₄COOC₆H₅ (V) →
4-(CH₃)₂NCH₂CH₂OC₆H₄COOC₆H₅ (VI) → IV. In addition,
4-NH₂C₆H₄CH(C₆H₅)OCH₂CH₂N(CH₃)₂ (VII) has been synthesized

Card 1/8

CZECHOSLOVAKIA / Organic Chemistry--Synthetic organic chemistry. G-2

Abs Jour : Ref Zhur - Khimiya, No 14, 1959, No. 49483

by the scheme: $C_6H_5NHCOC_6H_5$ (VIII) + C_6H_5COCl (IX) \rightarrow
 $4-C_6H_5CONHC_6H_4COC_6H_5$ (X) \rightarrow $4-C_6H_5CONHC_6H_4CH(OH)C_6H_5$
 (XI) \rightarrow $4-C_6H_5CONH-C_6H_4CH(C_6H_5)OCH_2CH_2N(CH_3)_2$ (XII) \rightarrow
 VII. Attempts to synthesize $4-NO_2C_6H_4CH(C_6H_5)OCH_2$
 $CH_2N(CH_3)_2$ (XIII) proved unsuccessful: $4-NO_2C_6H_4COC_6H_5$
 (XIV) is reduced with $LiAlH_4$ to $4-NO_2C_6H_4CH(OH)C_6H_5$ (XV);
 however, the reaction of XV with III apparently yields
 $4-C_6H_5COC_6H_4N(O)NC_6H_4COC_6H_5-4'$ (XVI) rather than XIII.
 Attempts to carry out the bromination of $4-NO_2C_6H_4CH_2C_6H_5$
 (XVII) (obtained by Friedel-Crafts synthesis from
 $4-NO_2C_6H_4COCl$ and C_6H_6 ; bp $145 - 149^\circ/0.2$ mm) to obtain
 $4-NO_2C_6H_4CH-(Br)C_6H_5$ gave XIV instead. The same result
 is obtained from the reaction of XV with PBr_3 . 29.7
 gms V in 50 ml abs NC_5H_5 are treated with 15 gms CH_3COCl

Card 2/8

G-6

CZECHOSLOVAKIA / Organic Chemistry--Synthetic organic chemistry. G-2

Abs Jour ; Ref Zhur - Khimiya, No 14, 1959, No. 49483

over 15 min (the temperature rises from 60 to 65°), the solution is stirred while cooling, 200 ml ice water are added, the solution is acidified with 80 ml conc HCl and 4-CH₃COOC₆H₄-COOC₆H₅ (XVIII) is isolated, yield 93%, mp 81° (corrected; from alc). 26.5 gms XVIII in 200 ml CH₃OH are hydrogenated over 5 gms Raney Ni (20°, 90 atm, 1.5 hrs, 2.8 liters H₂), and II is isolated from the filtrate, yield 82%, bp 155 - 160°/0.2 mm. 7.3 gms II, 3.8 gms III, and 2 gms of 70% NaNH₂ solution in 40 ml abs C₆H₆ are refluxed for 7 hrs, 100 gms ice and 15 ml conc HCl are added on cooling, the solution is extracted with ether, the aqueous layer is made alkaline with 40% NaOH and extracted with ether to give I, 44% yield, bp 163 - 165°/0.4 mm, picrate (PC) mp 150° (corrected; from alc). 17 gms V are added to a

Card 3/8

CZECHOSLOVAKIA / Organic Chemistry--Synthetic organic chemistry. G-2

Abs Jour : Ref Zhur - Khimiya, No 14, 1959, No. 49483

solution of 1.95 gms Na in 50 ml abs alc, the solution obtained is refluxed for 1 hr, 18 gms III are added on cooling, the solution is heated for 6 hrs at about 100°, the filtrate is evaporated under vacuum, the residuo is made alkaline with 40% NaOH and extracted with ether to give 17% VI, bp 170 - 172°/0.3 mm, PC mp 154 - 155° (from aqueous alc). 2 gms VI in 50 ml abs ether at about 20° are treated with 0.57 gm LiAlH₄ in 50 ml ether (added dropwise), the solution is stirred for 1 hr at about 20°, refluxed for 1 hr, decomposed by adding 10 ml water and 10 ml of 40% NaOH; the ether layer yields 41% IV, mp 83 - 84° (from petroleum ether), PC mp 117 - 118° (from aqueous alc). 100 gms VIII and 70 gms IX are heated to 180°, 50 gms of anhydrous ZnCl₂ are added over 10 min, and the melt is

Card 4/8

G-7

CZECHOSLOVAKIA / Organic Chemistry--Synthetic organic chemistry. G-2

Abs Jour : Ref Zhur - Khimiya, No 14, 1959, No. 49483

immediately poured into cold water; the substance which separates is dissolved in 750 ml alc and 700 ml water to give 34% X, mp 151° (corrected; from alc). 34 gms X in 1.5 liter alc are reduced with amalgam (7 gms Na and 250 gms Hg) at 15°, the solution is left to stand 48 hrs at about 20°, 3 liters water are added to the filtrate, and XI is isolated, yield 82%, mp 157° (corrected; from ethyl acetate). 9.1 gms XI, 3.8 gms III, and 2 gms 70% NaNH₂ in 60 ml C₆H₆ are refluxed for 7 hrs, 100 gms ice and 15 ml conc HCl are added on cooling, the solution is washed [sic] with ether, the aqueous layer is made alkaline with 40% NaOH, extracted with ether, the solvent is removed, and 9.4 gms of the residue are converted to the PC of XII, mp 170° (corrected; from acetone-ether); the PC

Card 5/8

CZECHOSLOVAKIA / Organic Chemistry--Synthetic organic chemistry. G-2

Abs Jour : Ref Zhur - Khimiya, No 14, 1959, No. 49483

is hydrolyzed with 15 ml (1 : 1) HCl, the $(\text{NO}_2)_3$ -
 $\text{C}_6\text{H}_2\text{OH}$ is removed with $\text{C}_6\text{H}_5\text{NO}_2$ and ether, the aqueous
 layer is made alkaline, and extracted with ether to give
 XII (0.9 gms). 4.4 gms of crude XII, 6 ml water, and
 0.9 gm NaOH are refluxed for 6 hrs, the solution is
 evaporated under vacuum, mixed with 30 ml water and
 30 ml ether, the ether layer is evaporated, the residue
 is dissolved in 40 ml N 7 HCl, the resulting solution
 is washed [sic] with ether, made alkaline with 40%
 NaOH, and extracted with ether to give 0.65 gm VII,
 bp 220 - 230°/0.3 mm. 14 gms XIV in 50 ml abs
 tetrahydrofuran (XIX) are treated over 30 min at $\leq 50^\circ$
 with a titrated [standardized?] solution of 0.63 gm
 LiAlH_4 in 90 ml XIX, the solution is stirred for an

Card 6/8

G-8

CZECHOSLOVAKIA / Organic Chemistry--Synthetic organic chemistry. G-2

Abs Jour : Ref Zhur - Khimiya, No 14, 1959, No. 49483

additional 30 min, hydrolyzed with 200 ml water and 30 ml (1 : 1) HCl, evaporated under vacuum, and the residue is extracted with ether to give 84% yield of XV, mp 74° (from C₆H₁₄). 5.7 gms XV, 3.2 gms III, and 1.6 gms 70% NaNH₂ in 30 ml C₆H₆ are refluxed for 7 hrs, the solution on cooling is hydrolyzed with 50 ml water, diluted with 100 ml C₆H₆ to give 61% XVI, mp 205° (corrected; from dioxane). 21.3 gms XVII at 160° are treated over 30 min with 18.7 gms Br₂, the solution is heated for 3 hrs at 160°, and diluted with 50 ml C₆H₆ to give XIV, bp 170 - 190°/1 mm. 5.9 gms SV and 4.5 gms PBr₃ are mixed at 0°, the solution is allowed to stand about 12 hrs at about 20°, followed by 2 hrs at about 100°, hydrolyzed with 50 ml water and extracted with 50 ml C₆H₆ giving 6.8 gms XIV, mp

Card 7/8

CZECHOSLOVAKIA / Organic Chemistry--Synthetic organic chemistry. G-2

Abs Jour : Ref Zhur - Khimiya, No 14, 1959, No. 49483

138° (corrected; from benzene- C_6H_{14}). For Communication
XLII see RZhKhim, No 23, 1958, 77702. -- V. Skorodumov

Card 8/8

G-9

COUNTRY : Czechoslovakia
 CATEGORY : Organic Chemistry—Synthetic organic chemistry
 ABS. JOUR. : RZKhlm., No. 16 1959, No. 57137
 AUTHOR : Jilek, J. O. and Protiva, M.
 INST. : Not given
 TITLE : Antihistamine Compounds. XLIV. Some New Salts of Mefenhydramine and Antazoline
 ORIG. PUB. : Ceskoslov Farmac, 7, No 8, 453-454 (1958)
 ABSTRACT : The following acid salts of I were prepared by the evaporation under vacuum at about 100° of a solution of 1.35 gm mefenhydramine, $(C_6H_5)_2C(CH_3)OCH_2CH_2N(CH_3)_2$, (I) and organic acids in 6 ml alcohol (the acid, yield of salt in gms, and the mp in °C are given in that order): 6 gms succinic, 1.35, 104° (from ethyl acetate); 0.75 gm d-tartaric, 1.65, 116-117 (from alc); 0.95 gm citric, 1.95, 130-132 (from abs alc). The above salts hydrolyze nearly as rapidly as the

CARD: 1/4

123

57137

COUNTRY : Czechoslovakia
CATEGORY :

ABS. JOUR. : RZKhim., No. 16 1959, No.

AUTHOR :
INST. :
TITLE :

GRIG. PUB. :

ABSTRACT :

hydrochloride of I. Antazoline, $C_6H_3CH_2N(C_6H_5)-CH_2C\equiv NCH_2CH_2NH$, (II) yields the following salts:
A solution of 5.3 gms II in 30 ml alc and
a solution of 1 gm H_2SO_4 in 5 ml alc are mixed
together to give the ethyl sulfate of II, mp
195° (corr; from alc); 2 gms H_2SO_4 in 7 ml iso-
 C_4H_7OH are added with cooling to a solution of
5 gms II in 15 ml iso- CH_3H_7OH or a solution of
2.2 gms H_2SO_4 in 5 ml C_6H_5OH is added dropwise
to a cold solution of 5 gms II in 15 ml n- C_4H_9OH

CARD: 2/4

COUNTRY : Czechoslovakia
CATEGORY :

G-2

ABS. JOUR. : RZKhim., No. 16 1959, No.

57137

AUTHOR :
INST. :
TITLE :

ORIG. PUB. :

ABSTRACT : give II. H_2SO_4 , yield 4.5 and 6.6 gms, respectively, mp 166-167° (corr; from iso- C_8H_7OH); 17 gms II are dissolved at 70° in a solution of 8 gms H_2SO_4 in 68 ml water, and the solution is allowed to stand 12 hrs, after which 17 gms II. $H_2SO_4 \cdot 0.5H_2O$ are obtained, mp 102° (washed with acetone and dried by distilling part of the $CHCl_3$ from a suspension of the salt in $CHCl_3$); 5.3 gms II are dissolved in a solution of 1 gm H_2SO_4 in 50 ml water and the solution

CARD: 3/4

124